Remarks

Claims 11-18 and 21-23 are currently pending. By the foregoing amendment, claims 10-13 and 21-22 have been amended and claims 1-10 and 19-20 have been cancelled. The specification has been amended to correct an error in spelling. All pending claims stand rejected.

Rejection under 35 U.S.C. 112 ¶1

The Examiner has rejected claims 10, 12, 14-18, 21 and 23 under 35 U.S.C. 112 ¶1 as failing to comply with the enablement requirement. The Examiner has confirmed that the art is silent with respect to the use of allithiamines, such as benfotiamine, in the prevention of aging or glycation. *See* Office Action p. 2, (2). However, with respect to those claims that recited the prevention of aging, the Examiner states that the art has set forth that aging cannot be completely prevented in any predictable manner. *See* Office Action p. 2, (4). In response, Applicant has amended independent claims 12 and 21 to remove the language of "prevention of aging" and directed these claims to the "prevention of damage" and "treatment of glycation," respectively. Applicant respectfully asserts that the rejection with respect to the recitation of "prevention of aging" has been traversed.

Further, the Examiner states that the claims are very broad in that they recite the prevention of aging/or glycation as entirely attributable to the administration of an allithiamines such as benfotiamine.,(*see* Office Action p. 3 (5)) and that the specification does not present aging and/or glycation can be entirely prevented due to the administration of the composition of the present invention. Applicant asserts that by the foregoing amendments, none of the claims recite the prevention of aging or the prevention of glycation. All claims, as amended herein, are either directed to reduction of glycation (claim 10), the treatment of glycation (claims 11 and 21), the treatment of aging (claims 13 and 22), or the prevention of damage (claim 12). Further, all claims

include as an element of all pending claims that the composition is "effective to reduce [or prevent] formation of glycated proteins." (Applicant's claims do not recite the prevention of glycation entirely.)

Applicant submits the specification is enabling for all of the amended claims. It is known in the art that allithiamines such as benfotiamine prevent the combination of sugars with proteins, and are used is treatments for nerve conditions sciatica and diabetic neuropathy, where diabetics who are extremely sensitive to sugar to the point where they experience nerve damage. The application details the chemical mechanism of sugars combining with proteins to cause glycation damage, which is known in the art at least in relation to diabetic nerve conditions. See Application ¶¶ **[0003]-[0006].** (Channeling of triosephosphates into a safe metabolic pathways mediated by the enzyme transketolase results in the production of harmless metabolites rather than damaging advanced glycation endproducts ("AGEs").)

Distinct from treating or preventing nerve damage, Applicant has discovered a method of use of applying a composition comprising benfotiamine to skin, which treats damaging effects, both immediate and multiplied later-on, caused by the presence and formation of glycated proteins. Hence, the invention, prevents the formation of glycated proteins ultimately to reduce the amount of glycated end-products presently in the skin (to treat the current condition and relieve existing damage), and also to prevent an increase in the amount by preventing future formation leading to future damage. *See* Application¶ **[0009]** (details effects of glycated proteins on skin). As stated in the Application,"[w]hile use of benfotiamine is known in the treatment of nerve conditions, its glycation-reducing effects have not been utilized in topical applications nor in treatments for skin conditions." See Application ¶ **[0006].**

Applicant respectfully asserts that foregoing amendments and remarks show enablement of the pending claims, traversing the §112 ¶1 rejection.

Rejection under 35 U.S.C. 103(a)

The Examiner has rejected claims 1-23 under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Runge *et al.* and Woerwag *et al.*, repeating the rejection from the prior Office Action received in this Application.

The Examiner states that there is insufficient disclosure that significantly differentiate between the condition disclosed by the prior art and that which is recited in the instant claims. Specifically, the Examiner states that the symptoms recited by the Applicant due to glycated proteins, such as inflammation, irritation, and uneven coloring are also symptoms shared by conditions disclosed in the prior art, such as rheumatic disorders and shingles. Applicant respectfully disagrees. Applicant discloses symptoms resulting from the breakdown of collagen and elasticity of the skin caused by the presence of glycated proteins. Immediate effects are disclosed as inflammation, wrinkles, and brown spots or lipofuscin, and later effects of inflammation, irritation, and erythema caused by toxic free radicals which are produced over time by glycated proteins. See Application ¶ **[0009]**. Once these damaging effects are lifted, elasticity and a supple feeling is returned to the skin; fine lines and wrinkles are lightened and skin coloring evens out. In contrast, Woerwag *et al.* discloses topical uses of benfotiamine for treatment of rheumatism and joint and neurological disorders which incidentally has temporal symptoms that manifest on the skin such as shingles, which is a temporal symptom of a dormant viral infection of the nerves. It does not teach or suggest a method of use of benfotiamine wherein the composition reduces or prevents the formation of glycated proteins.

Further, even if ***arguendo***, Woerwag was disclosed for a treatment of shingles (rather than the underlying nerve disorder), shingles does not display as inflammation, irritation, and uneven coloring despite the Examiner's contentions of such

characteristics. In fact, the characteristics of shingles are known as ranging from itching to extreme and intense pain. After several days, a rash appears beginning as a band or patch of raised dots on the side of the trunk or face. It then develops into small, fluid-filled blisters which begin to dry out and crust over within a few days. The rash and pain usually disappear within three to five weeks. Painful blisters, and even simply mild itchiness, are not symptoms similar to the effects of glycated proteins in the skin as disclosed by the Applicant. Further, it may be important to treat the underlying shingles virus at times when it leads to eye damage that could result in blindness and other complications such as partial facial paralysis, ear damage or encephalitis (inflammation of the brain), and otherwise in the form of a rash, it is typically not treated. Woerwag *et al.* addresses treatment of a virus which has pronounced symptoms and complications. There is nothing in the disclosure that would lead one of skill in the art to use benfotiamine in a composition for beneficial treatment of the skin by reducing glycation, preventing damage caused thereby, or treating aging caused thereby, by applying a composition comprising an effective amount of benfotiamine, wherein the composition reduces [prevents] formation of glycated proteins.

The disclosure is Woerwag *et al* addresses treatment and amelioration of the nerve disorders (and the underlying viral infection), and while some of them may include symptoms appearing upon the skin, such as shingles, Woerwag *et al* does not teach or suggest benfotiamine for improvement of skin, wherein the composition reduces or prevents formation of glycated proteins as in the present claims. Further, this element of the present claims is not taught or suggested by Runge which includes a cursory disclosure of benfotiamine as one of several potential adjunct ingredients in carotenoid formulations for cosmetic preparations and supplements. (*See* Runge col. 3, lines 3-4).

In Runge *et al.*, there is no discussion of the properties or effects of benfotiamine alone or when incorporated with any of these other several listed potential adjunct ingredients. There is no disclosure or suggestion to the method of use of an effective

Clean copy of the replacement paragraph for the specification

[0005] These damaging reactions may be prevented by channeling of triosephosphates into a safe metabolic pathway mediated by the enzyme transketolase and producing harmless metabolites rather than damaging AGEs. As thiamin (B12) is the cofactor that works with the enzyme transketolase and essentially activates it, thiamin is believed to prevent AGE formation and resulting cell damage. As benfotiamine is a highly absorbable, it effectively increases the levels of thiamin in cells and the resulting transketolase activity that shields cells from AGE damage.

amount of benfotiamine in a topical composition to improve skin condition, wherein the composition reduces or prevents formation of glycated proteins as in claimed by Applicant. Hence, Neither Woerwag *et al.* or Runge *et al.*, alone or in combination, teach or suggest the methods as claimed in the present invention.

Applicant respectfully asserts that in light of the foregoing amendment and remarks, the Response renders all pending claims in condition for allowance, and early notice of such is requested.

Respectfully submitted,

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